PATENT
Attorney Docket No. BNIT0003-PCT-US

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

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| In re Application of: | ) | |
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| Søren Mouritsen et al. | ) | Group Art Unit: 1644 |
| | ) | |
| Application No.: 08/955,373 | ) | Examiner: SCHWADRON, Ronald B. |
| | ) | |
| Filed: October 21, 1997 | ) | |
| | ) | |
| For: INDUCING ANTIBODY RESPONSE AGAINST SELF-PROTEINS WITH THE AID OF FOREIGN T-CELL EPITOPES | ) | Confirmation No.: 7254 |
| | ) | |

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Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir or Madam:

**RESPONSE TO NOTICE OF NON-COMPLIANT APPEAL BRIEF UNDER 37 C.F.R. §47.37**

Applicants hereby respond to the Notice of Non-Compliant Appeal Brief ("Notice") mailed June 20, 2012, and setting a period comprising the longer of one month or 30 days to respond. Notice, page 2, item 2. Accordingly, this response is timely filed on or before Friday, July 20, 2012.

The Notice indicates that "[t]he brief does not contain a concise explanation of the subject matter defined in each of the rejected independent claims, referring to the specification in the Record by page and line number or by paragraph number and to the drawings, if any, by reference characters."

In particular, the Office asserts that the brief is non-compliant because "Section III Summary of Claimed Subject Matter does not refer to the Specification as originally filed with respect to independent claim 102, i.e. refers to paragraph numbers but the Specification as originally

filed does not include paragraph numbers." Notice, page 2, item 4. The Notice further indicates that "[a]nother appeal brief in its entirety is not required, just the deleted sections may be submitted." Notice, page 2, item 4.

Applicants note that the section entitled "Summary of Claimed Subject Matter" is actually Section V of the Appeal Brief as-filed, not Section III as indicated in the Notice. Applicants understand from the Office that the Notice refers to Briefs filed in a new, shorter format omitting Sections III (Status of the Claims) and IV (Status of Amendments) of the old format, resulting in the renumbering of sections in the Appeal Brief as-filed such that originally-filed Section V would become Section III in the new format. Because Applicants need not refile the entire Appeal Brief, however, we therefore submit herewith a corrected "Summary of Claimed Subject Matter" labeled as "Section V" in accord with the old Appeal Brief format, and in which the citations to the US Patent Publication corresponding to the present application have been replaced with citations to the specification as originally-filed.

Please replace "Section V: Summary of Claimed Subject Matter" of the Appeal Brief filed June 11, 2012, with the enclosed corrected section.

Applicants also note that, while the present application was filed on October 21, 1997, it was a file-wrapper continuation of a previously-filed application, so that filing did not include a copy of the specification. Consequently all citations to the specification as originally-filed refer to the copy of the specification filed June 7, 1995, and assigned US Application No. 08/477,501. *See, e.g.*, Miscellaneous Incoming Letter of October 21, 1997, page 2 (instructing the Office to use the contents of the prior application (US Application No. 08/803,321) file wrapper as the basic papers for the new application); Miscellaneous Incoming Letter of February 21, 1997, page 2 (instructing the Office to use the contents of the prior application (US Application No. 08/477,501) file wrapper

as the basic papers for the new application); and Transmittal of New Application of June 7, 1995, page 1 (referencing the originally-filed specification).

Please grant any extensions of time required to enter this response and charge any additional required fees to Deposit **Account No. 50-5338**, referencing **Docket No. BNIT0003-PCT-US**.

Respectfully submitted,

Dated: June 22, 2012

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**CORRECTED SECTION**

## V. Summary Of Claimed Subject Matter

Independent claim 102 is directed to a method for inducing autoantibodies against a self-protein in a subject. The claimed method comprises a step of administering an analog of the self-protein made by molecular biological means, according to which one or more peptide fragments of the self-protein are substituted with one or more immunodominant foreign T-cell epitopes. The substitutions are made such that the secondary and tertiary structure of the self-protein is preserved to a large extent, in this manner creating a modified self-protein analog that induces an autoantibody response in the subject as shown by the production of antibodies which bind to the unmodified self-protein. The immunodominant foreign T-cell epitopes to be substituted for self-protein sequences are selected from those in ovalbumin, hen egg lysozyme, tetanus toxoid or diphtheria toxoid.

Dependent claims 103, 105, and 111 are drawn to specific embodiments of the method in which the one or more immunodominant foreign T-cell epitopes is an ovalbumin T-cell epitope generally (claim 103) or a specific ovalbumin T-cell epitope (claim 105), and in which the self-protein is tumor necrosis factor-alpha ("TNFα").

The claimed subject matter, with its functional limitation, finds support throughout the specification originally-filed as US Application No. 08/407,551 ("the '551 application"), for example at:

> Page 3, lines 26-30, disclosing that the surprising observations underlying the claimed invention are a consequence of the fact that the immunodominant foreign T-cell epitopes are inserted into the self-protein, against which it is the purpose to raise antibodies, in such a way that they substitute for the self-protein fragments, thereby preserving the overall secondary and tertiary structure of the self-protein to a large extent;
>
> Page 4, line 31 to page 5, line 1, disclosing that the immunodominant foreign T-cell epitopes can be derived from tetanus toxoid;

Page 5, line 32, to page 6, line 8, disclosing that the substitution by molecular biological means of one or more peptide fragments in a self-protein by a corresponding number of immunodominant foreign T-cell epitopes in such a way that the tertiary structure of the self-protein is essentially preserved renders the resulting self-protein analog highly immunogenic, leading to the induction of a profound antibody response against the unmodified self-protein that is not restricted to the known major histocompatibility complex ("MHC") type of the inserted immunodominant foreign T-cell epitopes;

Page 8, line 33, to page 9, line 6, disclosing the preparation of self-protein analogs of ubiquitin and TNFα by the insertion of foreign T-cell epitopes 12-15 amino acids in length using genetic engineering methods and purification of such analogs, as well as production of autoantibodies against both ubiquitin and TNFα within one week after injection of the self-analogs emulsified in adjuvant into mice (*see also* Example 2 (page 11, line 25, to page 12, line 16) and Figures 1-2; as well as Example 3 (page 12, line 18, to page 13, line 33) and Figures 3-4);

Page 9, lines 19-29, disclosing analogs of the self-proteins ubiquitin and TNFα produced by substitution of one or more peptide fragments by a corresponding number of peptides known to contain immunodominant T-cell epitopes, where the substitution is carried out so as to essentially preserve the overall tertiary structure of the original self-protein, and that it was possible to induce a fast and strong autoantibody response against such self-protein analogs even though the inserted foreign T-cell epitope was not restricted to the MHC molecules of the immunized mice;

Original claim 5 (page 19, lines 22-23), disclosing that the immunodominant foreign T-cell epitopes can originate from tetanus toxoid or diphtheria toxoid;

Example 1 (page 11, lines 10-23), disclosing molecular biological means for producing various self-protein analogs used in the claimed method;

Example 2 (page 11, line 25, to page 12, line 16) and Figures 1-2, disclosing the cloning strategy for producing ubiquitin analogs modified to include immunodominant foreign T-cell epitopes derived from ovalbumin or hen egg lysozyme, the purification of such analogs and their administration to mice, and the production of ubiquitin autoantibodies; and

Example 3 (page 12, line 18, to page 13, line 33) and Figures 3-4, disclosing the cloning strategy for producing TNFα analogs modified to include immunodominant foreign T-cell epitopes derived from

ovalbumin or hen egg lysozyme, the purification of such analogs and their administration to mice, and the production of TNFα autoantibodies.